Published in final edited form as:

Int J STD AIDS. 2012 April ; 23(4): 242–247. doi:10.1258/ijsa.2011.011193.

Human papillomavirus prevalence, cervical abnormalities and risk factors among female sex workers in Lima, Peru

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Summary

Female sex workers (FSWs) are at high risk of human papillomavirus (HPV) infection. Questionnaires were administered to 200 FSWs aged 18–26 years in Lima, Peru, to gather risk behaviours, and cervical swab samples were collected for Pap smears and HPV DNA testing as part of a longitudinal study. Participants reported a median of 120 clients in the past month, and 99.2% reported using condoms with clients. The prevalence of any HPV in cervical samples was 66.8%; 34 (17.1%) participants had prevalent HPV 16 or 18, and 92 (46.2%) had one or more oncogenic types. Fifteen women had abnormal Pap smears, 13 of which were HPV DNA positive. Fewer years since first sex was associated with oncogenic HPV prevalence in a model adjusted for previous sexually transmitted infection (STI) status and condom use with partners (prevalence ratio = 0.77, 95% confidence interval [CI] = 0.60–0.97). Our data confirm the high rates of HPV transmission among FSWs in Peru, highlighting the need for early and effective strategies to prevent cervical cancer.

Keywords

human papillomavirus; HPV infection; female sex workers; cervical abnormality; sexually transmitted infection; STIs; Peru

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INTRODUCTION

Approximately 500,000 women develop cervical cancer each year worldwide and persistent human papillomavirus (HPV) infection is found in nearly all cases.¹ HPV among women with normal cytological findings is high and variable across world regions.² HPV prevalence among women in Peru is 17.7%, nearly twice the worldwide rate, and cervical cancer is the leading cause of cancer deaths in Peruvian women.^{3,4} Female sex workers (FSWs) are presumably at higher risk of HPV infection and cervical cancer compared with women in the general population due to their exposure to multiple sexual partners.^{5,6} Prevalence of HPV among FSWs ranges from 2.3% to 100.0%, with a median of 26%.^{7,8} Reports of prevalence of oncogenic HPV infection ranges from 12.7% to 44.5% among FSWs in the Americas.^{8,9}

HPV vaccines are highly efficacious against cervical intraepithelial neoplasia (CIN) associated with types 16 and 18 in women who were not infected at the time of immunization.¹⁰ HPV vaccines are approved for use in the general population of women aged 9–26 years in more than 100 countries, but FSWs were not included, as a group, in the clinical trials. Only 10% of FSWs in Lima were aware of the vaccine.¹¹ Vaccination of brothel-based FSWs at their point of entry into sex work could potentially lower their burden of cervical cancer and decrease transmission to their sexual partners and clients. While it is ideal to vaccinate prior to the onset of sexual activity, all women could potentially benefit from vaccination, with the absolute benefit dependent on the extent of prior infection. We estimated the prevalence of HPV genotypes, Pap smear abnormalities and risky sexual behaviours among FSWs from Lima to evaluate the potential benefit in a study targeting brothel-based FSWs for HPV vaccination.

METHODS

Subjects

FSWs 18–26 years of age were recruited between 28 August 2009 and 3 March 2010 from 49 different locales in Lima, Peru by trained medical staff and eight health promoters. Potential participants provided verbal consent to undergo a brief screening in a private area at their place of work. Inclusion criteria were age 18–26 years, registered as a FSW living in Lima, no reported immune deficiency (including HIV), not pregnant or planning a pregnancy in the next seven months, having a uterus and not having received HPV vaccine. If they fulfilled inclusion criteria, women were asked to report to the study clinic during a date and time convenient for the participant for completion of surveys, vaccination, Pap smears and counselling.

The study was approved by the institutional review boards at the Universidad Peruana Cayetano Heredia, NGO Via Libre, Instituto Nacional de Salud of Peru and the Johns Hopkins Bloomberg School of Public Health.

Data collection

All participants provided written informed consent before participating in study procedures including four visits over seven months. Surveys consisted of 52 questions divided into nine

sections including demographic data, sexual health, condom use, HPV knowledge and barriers, and medical history. Study documents were translated from English to Spanish and a certificate of translation was provided. The survey was labelled with a unique identification number. All surveys were administered in Spanish by a trained interviewer and results were immediately checked for completion by a supervisor. Participants had a pregnancy test followed by a general physical and gynaecological exam. Endo- and ectocervical cell samples were collected via Pap smear and a cervical swab was collected for HPV DNA testing using the Digene HPV sampling kit (Qiagen Inc, Gaithersburg, MD, USA). Women with low-grade intraepithelial lesions (LSIL) or high-grade intraepithelial lesions (HSIL) were referred for biopsy and colposcopy; those with HSIL or persistent LSIL previously diagnosed over one year ago were referred for LEEP (loop electrosurgical excision procedure) to remove abnormal cervical tissues in accordance with Peruvian guidelines. Genital tract infections were defined as bacterial (bacterial vaginosis, urinary tract infection, cervicitis), fungal (candida), viral (herpes, HPV) or protozoal (trichomoniasis).

Analyses

Survey data were double entered into EpiInfo 3.5.1 (CDC, Atlanta, GA, USA) by study staff and checked for logic and range. Discrepancies were resolved using the source document. Stata 9.0 (Stata Corp, College Station, TX, USA) was used for quantitative data analyses. Pearson's chi-square tests were computed for differences in HPV infection by age. Fisher's exact test was used for small sample comparisons. Differences in means were computed by *F* test.

The association between years since first sex and overall, high-risk, and quadrivalent vaccine-associated HPV prevalence was evaluated using prevalence ratios (PRs) with Poisson regression. Individual variables associated or nearly associated ($P < 0.2$) with HPV prevalence were considered in our final models.

Cervical samples were analysed for the presence or absence of HPV DNA by polymerase chain reaction using PGMY09/PGMY11 primers at Johns Hopkins Bloomberg School of Public Health.¹² Roche Linear Array genotyping (Roche Diagnostics, Indianapolis, IN, USA) testing detected 37 HPV types including oncogenic (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 66) and non-oncogenic types (6, 11, 26, 40, 42, 53, 54, 55, 61, 62, 64, 67, 68, 69, 70, 71, 72, 73, 81, 82, 82var, 83, 84 and 89) as defined at the 2005 meeting of the International Agency for Research on Cancer.¹³ Pap smears were read by a pathologist and reported using the Bethesda system.¹⁴

RESULTS

Study population

Of 599 women approached, 200 (33%) were enrolled (Figure 1). A cervical sample was not available for one participant. The average age of the 199 study participants was 23 years and 162 (81%) were Peruvian nationals (Table 1). Other participants were from Bolivia, Brazil, Columbia, Ecuador and the Dominican Republic. Seventy percent of women had heard of

HPV at the time of the study, and of those, 94% responded that women can be infected with HPV, and 88% knew of a vaccine to prevent cervical cancer.

Ninety-nine percent of women reported using a method to prevent pregnancy; 24% used oral contraceptives in addition to condoms. The mean percentage of reported condom use in the past month was 99.2% with clients and 29.7% with partners. HPV prevalence was associated with reported condom use with clients (prevalence ratio [PR] = 0.68, 95% confidence interval [CI] 0.53–0.86) but not with partners (PR = 0.88, 95% CI 0.66–1.17). The number of sexual encounters with non-paying partners in the past month for those who reported having a non-paying partner (mean 9.58, range 0–60) was marginally associated with HPV prevalence (PR = 0.99, 95% CI 0.98–1.00).

Twenty-seven percent of women reported having had a genital tract infection diagnosed in the past 12 months including bacterial ($n = 41$), fungal ($n = 2$), viral ($n = 11$) and protozoal ($n = 1$), and diagnosis of cervicitis was reported by 51% of participants with these infections. HPV ($n = 8$) and genital herpes ($n = 3$) were reported by 5.5% of participants. Having had a genital tract infection in the past year was not associated with any HPV prevalence (PR = 1.09, 95% CI 0.88–1.34), but was marginally associated with prevalent oncogenic HPV (PR = 1.33, 95% CI 0.98–1.80) (Table 2). Upon physical examination, 93 women (47%) had vaginal discharge and 55 (28%) had cervical inflammation.

HPV prevalence and cervical abnormalities

Among the 199 participants, the prevalence of one or more HPV DNA genotypes was 66.8%; 92 (46.2%) were positive for at least one oncogenic HPV, and 107 (53.8%) were positive for at least one lower risk HPV genotype. Vaccine-associated genotype prevalence included HPV 6 ($n = 11$, 5.5%), HPV 11 ($n = 1$, 0.5%), HPV 16 ($n = 28$, 14.1%) and HPV 18 ($n = 6$, 3.0%) (Figure 2). HPV prevalence was high in all women aged 19 years and the highest rate of abnormal Pap smears was in women 18 years old. Women aged 22 years had the highest proportion of oncogenic HPV (66.7%).

Of the 15 abnormal Pap smears, five were atypical squamous cells of unknown significance, seven were LSIL and three HSIL (Figure 3). Ten women underwent colposcopy and biopsy for LSIL or HSIL detected in Pap, and six women with histologically confirmed HSIL or persistent LSIL underwent LEEP. HPV 16 was detected in all participants who underwent LEEP. Ten participants had genital warts, five in whom the warts were perineal, and genital warts were always treated with cryotherapy. Of women with LSIL or HSIL, 100% had one or more oncogenic HPV types versus 43% for women with a normal Pap (PR = 2.30, 95% CI 1.96–2.71). The prevalence of vaccine-associated genotypes was 21% among women with a normal Pap result, compared with 60% for those with LSIL or HSIL (PR = 2.84, 95% CI 1.59–5.05).

Risk factors for HPV prevalence

Factors associated with prevalent HPV infection included age at first sex >17 years (PR = 1.3, 95% CI = 1.11–1.60), previous pregnancy (PR = 1.26, 95% CI = 1.04–1.54), fewer years since first sex (PR = 0.81, 95% CI = 0.70–0.94) and age at first period >14 years (PR

= 1.22, 95% CI = 1.02–1.54). Overall age was not associated with prevalent HPV (PR = 1.91, 95% CI = 0.81–1.07). Women with oncogenic HPV (PR = 0.75, 95% CI = 0.56–1.01) or with any HPV (PR = 0.80, 95% CI = 0.65–0.97) were significantly more likely to have fewer years since sexual debut compared with women without HPV.

Variables considered in our final models included ever being pregnant, age at first period, age at first sex, having a sexually transmitted infection (STI) in the past year, having a nonpaying sexual partner, condom use with partners and condom use with clients (Table 2). Having lost a pregnancy and frequency of non-paying sexual partner intercourse without condoms were dropped from the multivariate models due to collinearity.

In the univariate models, years since first sex ($P < 0.01$) and age at first period ($P = 0.04$) were associated with any HPV infection, while years since first sex ($P = 0.03$), previous STIs ($P = 0.06$) and condom use with non-paying partners ($P = 0.05$) were associated with oncogenic HPV. Years since first sex was significantly associated with oncogenic HPV infection ($P = 0.03$) in a model adjusted for prevalent STIs in the past year and condom use with partners. Years since first sex was associated with any HPV infection ($P = 0.02$) in a model adjusted for age at first period.

DISCUSSION

High point prevalence of HPV genotypes highlights a high sexual exposure to HPV among FSWs in this study despite reported consistent condom use. Presence of Pap smear abnormalities was lower than expected, but may be explained with the low sensitivity of the cytology screening in Peru. Vaccination should occur among young Peruvian women to ensure future protection against vaccine-associated genotypes, particularly in future high-risk groups.

Rates of condom use in our study were higher than reported rates among FSWs in Africa and the eastern Mediterranean, where condom use with clients was less than 50%.¹⁵ Condom use is a requirement for FSWs in licensed Peruvian brothels, thus FSWs may have over-reported condom use in our study to appear compliant with government regulations. Despite reporting high rates of condom use with clients, FSWs in Lima have a high prevalence of HPV and other STIs.¹⁶ One-quarter of participants in our study reported having had an STI diagnosis in the past year, which could be consistent with potential over-reporting of condom use, or could suggest that women contracted STIs from their non-paying sexual partners.

The abnormal Pap prevalence in this study was less than half the 21.6% reported among Guatemalan FSWs, possibly due to the lower age and/or higher reported condom use among participants in our study.⁹ Alternatively, the quality of subjective Pap smear interpretation varies; the sensitivity of Pap smears for diagnosis of CIN 2/3 and cancer in a large study in the Peruvian Amazon was below 25%.¹⁷ Special efforts should be made to improve cervical cytology in Peru.

The prevalence of oncogenic HPV types among our study participants was higher than the 35.6% noted in a recent study of 87 Peruvian FSWs using line blot assay.¹⁸ Our high

prevalence of oncogenic types could be due to the higher number of genotypes we tested, our use of the more sensitive linear array testing, or our larger sample size.¹⁹ The overall HPV prevalence in this study is higher than that found in a large cohort of FSWs in Mexico city (48.9%), Indonesia (38.3%) and Spain (31.5%), perhaps resulting from the different sexual practices of women in each country and the variability in HPV testing including the use of linear array, line blot and hybrid capture 2.^{20–22}

There was a strong association between years since first sex and higher HPV prevalence. Women who were farther from their sexual debut may have acquired and cleared their infections prior to study enrolment, whereas women with a more recent sexual debut may be less likely to have cleared infections and/or acquired protective immunity. Previous studies of FSWs have shown an inverse relationship between age and HPV prevalence.^{18,20,21,23–25} The decreased prevalence with age may be due to clearance of infection or development of protective immunity. Age was not directly associated with HPV prevalence in our study, most likely due to the limited age range of our study participants.

Although our study participants were drawn from a variety of venues with different income levels in Lima, the results may not be representative of the entire FSW population in Lima. Some women did not have the opportunity to participate, refused to participate or did not meet our eligibility criteria; if non-participation was related to sexual behaviours or HPV prevalence, this could have biased our estimates. A larger sample size could have yielded significant results including an increased number of sexual encounters with non-paying partners in the past month and significantly more genital tract infections in the past year. In addition, we did not conduct HIV testing and relied on self-reports of HIV results. Estimates from 2008 show a total HIV prevalence of 0.32% in Peru, with 2.1% among FSWs.²⁶ Another limitation in this study is that all behavioural data are self-reported, and some responses may be a result of response bias.

The cumulative lifetime HPV exposure is undoubtedly higher than the point prevalence of HPV DNA observed in this study due to clearance of some infections. Serological testing could provide a better estimate of cumulative risk of HPV among these FSWs. Cohort studies would assist in understanding HPV epidemiology, and including HPV test results from oral, vulvar, perianal and anal samples would also provide a more complete picture of prevalent HPV infections.

The high point prevalence of HPV DNA in this population of young FSWs highlights the need to vaccinate girls early in order to maximize benefit and protection in high-risk populations. Vaccines should not take the place of Pap smears, but they should complement cervical cytology, particularly in areas similar to Peru with less than 50% of women of child-bearing age receiving Pap smears.²⁷ Seroprevalence of vaccine-associated types in this population will be important to estimate the potential effectiveness of HPV vaccination among FSWs starting sex work. The current high list price of HPV vaccines is prohibitive for widespread acceptance in developing countries. Private-public initiatives are needed to bring these much needed vaccines to all women throughout the world, including FSWs. The Gates Foundation, Program for Appropriate Technology in Health (PATH), and the International Agency for Research on Cancer (IARC) are working in this effort.^{28,29} If HPV

vaccination is found to have a favourable cost benefit in FSWs, retention activities should be strengthened to facilitate new FSWs receiving all three doses of vaccine.

ACKNOWLEDGEMENTS

The authors would like to thank study team members Lisbeth De la Rosa, Cristina Esteves, Isaac Alva and Juan Carlos Bartolo for their assistance in data collection. We would also like to thank the brothel managers and health promoters for their efforts, Tina Proveaux for administrative and editorial assistance and Yolanda Eby and Roslyn Howard for their technical assistance in HPV genotyping. Supported in part by a research grant from the Merck Investigator-Initiated Studies Program of Merck & Co Inc. The opinions expressed in this paper are of the authors and do not necessarily represent those of Merck & Co Inc. This research was funded, in part, by the Department of International Health Global Disease Epidemiology Program, Delta Omega Scholarship, Dan David Prize Scholarship, Carol Eliasberg Martin Scholarship in Cancer Prevention, NIH training grant number 5T32HD046405-03, NIH grant T32 MH080634, NIH Pre-doctoral National Research Service Award F31AI080187, Fogarty International Clinical (FIC) Research Fellows Program, FIC/NIH grant 1R01TW008398 and discretionary University funds.

Competing interests: NAH received financial compensation for serving on Safety Monitoring Boards for the post-licensure safety assessment evaluation of Gardasil and other vaccines produced by Merck within the past two years. He received no financial support for participation in this study.

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Figure 1.
Final study participants from initial eligibility screening. FSW = female sex worker

Figure 2.
Presence of 37 high- and low-risk HPV DNA genotypes among 199 female sex workers in Lima, Peru. HPV = human papillomavirus

Figure 3.

Management of Pap smear results. HSIL = high-grade intraepithelial lesions; LSIL = low-grade intraepithelial lesions; ASCUS = atypical squamous cells of unknown significance; LEEP = loop electrosurgical excision procedure

Table 1

Characteristics of 199 female sex workers in Lima, Peru, by HPV DNA results

	All participants, <i>n</i> (%)	HPV DNA positive, <i>n</i> (%)	HPV DNA negative, <i>n</i> (%)	<i>P</i> value for group differences [*]
Age (years)				
18–22	85 (42.7)	62 (72.9)	23 (27.1)	0.11
23 and above	114 (57.3)	71 (62.3)	43 (37.7)	
Heterosexual				
Yes	193 (97.0)	130 (67.4)	63 (32.6)	0.37
No	6 (3.0)	3 (50.0)	3 (50.0)	
Education completed				
Primary	17 (8.5)	10 (58.8)	7 (41.2)	0.30
Secondary	107 (53.8)	68 (63.6)	39 (36.4)	
Higher	75 (37.7)	55 (73.3)	20 (26.7)	
Marital status				
Single	120 (60.3)	83 (69.2)	37 (30.8)	0.84
Married	11 (5.5)	7 (63.6)	4 (36.4)	
Cohabiting	60 (30.2)	38 (63.3)	22 (36.7)	
Divorced/widowed	8 (4)	5 (62.5)	3 (37.2)	
Ever pregnant				
Yes	163 (81.9)	104 (63.8)	59 (36.2)	0.05
No	36 (18.1)	29 (80.6)	7 (19.4)	
Lost pregnancy				
Yes	124 (62.6)	78 (62.9)	46 (37.1)	0.15
No	74 (37.4)	54 (73.0)	20 (27.0)	
Age at first period				
9–13 years	122 (61.3)	75 (61.5)	47 (38.5)	0.04
14 years and above	77 (38.7)	58 (75.3)	19 (24.7)	
Years since first sex				
1–4 years	41 (20.6)	34 (82.9)	7 (17.1)	0.03
5–9 years	120 (60.3)	78 (65.0)	42 (35.0)	
10–14 years	38 (19.1)	21 (55.3)	17 (44.7)	
Mean clients in past month (range) [†]	165.8 (2–1800)	159.1 (2–1800)	178.9 (4–1400)	0.63 [‡]
Mean condom use with clients in past month (95% CI)	99.4 (98.4–100)	98.9 (97.4–100.0)	99.7 (99.3–1.00)	0.48
Has non-paying sex partners				
Yes	145 (72.9)	100 (69.0)	45 (31.0)	0.30
No	54 (27.1)	33 (61.1)	21 (38.9)	
Mean unprotected partner intercourses in past month (range) [†]	9.84 (1–70)	9.0 (6.71–11.3)	12.4 (7.0–17.7)	0.65 [‡]
Mean condom use with partners in past month (95% CI)	29.7 (22.7–36.7)	27.7 (19.6–35.9)	34.8 (20.8–48.9)	0.36 [‡]
Pap smear in lifetime				

	All participants, <i>n</i> (%)	HPV DNA positive, <i>n</i> (%)	HPV DNA negative, <i>n</i> (%)	<i>P</i> value for group differences [*]
Yes	166 (83.4)	110 (66.3)	56 (33.7)	0.70
No	33 (16.6)	23 (69.7)	10 (30.3)	
STI diagnosis in past year				
Yes	55 (27.6)	39 (70.9)	16 (29.1)	0.45
No	144 (72.4)	94 (65.3)	50 (34.7)	

Note: Some participants refused to answer questions in the survey

HPV = human papillomavirus; STI = sexually transmitted infection; CI = confidence interval

^{*} Fisher's Exact test was used or χ^2 *P* value unless otherwise noted

[†] Split at the median

[‡] Mean (95% CI) was used for calculation of group differences, and analysis of variance testing was done to test significance

Table 2

Prevalence ratios (PRs) and 95% CIs for the association between HPV prevalence, years since first sex, and other factors

	Any HPV infection		Oncogenic HPV infection	
	Univariate model PR (95% CI)	Final model PR (95% CI)	Univariate model PR (95% CI)	Final model PR (95% CI)
Years since first sex (years)				
1–4	Ref	Ref	Ref	Ref
5–9	0.78 (0.65–0.95)	0.82 (0.67–0.99)	0.72 (0.52–0.99)	0.73 (0.54–1.00)
10–14	0.66 (0.48–0.92)	0.69 (0.50–0.95)	0.60 (0.37–0.98)	0.60 (0.37–0.98)
Age at first period				
9–13 years	Ref	Ref	Ref	–
14 years and above	1.23 (1.01–1.48)	1.18 (0.97–1.42)	1.17 (0.86–1.57)	–
Previous STIs				
Yes	1.09 (0.88–1.34)	–	1.33 (0.98–1.80)	1.31 (0.97–1.75)
No	Ref	–	Ref	Ref
Condom use with partners				
None of the time	Ref	–	Ref	Ref
Some of the time	0.91 (0.75–1.10)	–	0.79 (0.59–1.07)	0.78 (0.59–1.05)

HPV = human papillomavirus; STI = sexually transmitted infection; CI = confidence interval